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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,634	12/14/2001	Ronenn Roubenoff	21629-004	1772

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/020,634	ROUBENOFF ET AL.	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11252003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. By Amendment filed January 16, 2004, claims 14-47 have been cancelled and claims 1-6 and 9-13 have been amended. Claims 1-13 are currently pending for prosecution on the merits.

2. Applicant's amendment necessitates a new ground of rejection(s) in this Office action.

Information Disclosure Statement

3. Acknowledgement is made of applicant's submitting of the information disclosure statement (IDS) on November 25, 2003. With respect to "PCT International Search Report dated November 4, 2002" in the submitted PTO-1449, the information disclosure statement filed November 25, 2003 fails to comply with 37 CFR 1.98(a)(1), which requires a list of all patents, publications, or other information submitted for consideration by the Office.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

4. Claim 1 are rejected under 35 U.S.C. 102(a) or 102(e) as being anticipated by Muller et al. (US 6011040).

Muller expressly teaches a composition comprising reduced folate compound (i.e., 5-formimino-(6S)-tetrahydrofolic acid and vitamin B (i.e., vitamin B12), wherein an amount of said reduced folate compound is in dose range between 0.001mg and 1000mg, and an amount of said vitamin B12 is in dose range of 0.001mg and 0.5mg (column 2, lines 19-25; column 3, lines 9-21 and lines 30-40; Example 10; claims 5, 19-20).

Although Muller is silent about the "a chondroprotective effect" of said composition, such characteristic or property must be inherently present in said composition. Especially, in view of the overlapping dosage range of the active ingredients (e.g., reduced folate compound such as 5-formimino-(6S)-tetrahydrofolic aci, and vitamin B12) in a composition over the prior art range, such functional characteristic or property of said composition is deemed to be inherent to the composition. Therefore, the reference anticipates the claimed invention.

5. Claims 2-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Smith (WO 98/19690).

This rejection is analogous to the original rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claim 10-13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (WO 98/19690).

The teaching of Smith has been discussed in above 35 USC 102(e) rejection.

The teaching of Smith differs from the claimed invention in (i) the use of a natural isomer of reduced folate (e.g., (6S)-tetrahydrofolic acid, 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic aicd, etc...) for preparing said composition; and (ii) the specific dosage amount of said folic acid or reduced folate compound in range of 150-1000mg.

One having ordinary skill in the art would have expected that the individual isomers are obvious variants over the corresponding racemate because of their presence in the racemate. It would further be expected that one of the isomers would be more active than the other and the

racemate would exhibit the combined effects. Thus, one having ordinary skill in the art would have been motivated to employ a natural isomer of reduced folate such as (e.g., (6S)-tetrahydrofolic acid, 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic aicd, etc...) to arrive at the claimed composition such that the pharmacological activity of said composition would be greatly enhanced.

With respect to the claimed dosage range of said compound, generally differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller, 220 F. 2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).*

Response to Arguments

7. Applicant's arguments filed January 16, 2004 have been fully considered but they are not persuasive.

In response to the rejection of the claims under 35 USC 102(b) rejection, applicants have amended claims 1 by requiring the claimed compound to either "5-formimino-(6S)-tetrahydrofolic acid or 5-formimino-(6R,S)-tetrahydrofolic acid", and overcame the rejection under 35 USC 102(b).

In response to the rejection of the claims under 35 USC 102(b) rejection, applicants have amended claim 2 by requiring the ratio of a reduced folate compound and cobalamine is between 50:1 and 125:1. However, since the referenced ratio of <u>about 50:1</u> reads on the lower limit of the

instantly amended ratio of reduced folate to cobalamine, "50:1 to 125:1", the examiner maintains that the reference anticipates the claimed invention.

In response to the rejection of the claims under 35 USC 102(b) rejection, applicants have amended claim 11 by requiring "the composition contains between 150-1000mg of a reduced folate", and overcame the rejection under 35 USC 102(b).

In response to the rejection of the claims under 35 USC 103(a) rejection, applicants have amended claim 10 by requiring "the ratio of reduced folate to cobalamine is between 50:1 and 125:1". However, as discussed above, the referenced ratio of about 50:1 reads on the lower limit of the instantly amended ratio of reduced folate to cobalamine, "50:1 to 125:1", the examiner maintains that the reference makes obvious the claimed invention.

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. No Claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (571) 273-0584. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614

ZOHREH FAY
PRIMARY EXAMINER
GROUP 1600